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October 15, 1992

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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91 CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

mm

2/15/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation's TSCA §8(e) reporting standard². This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.³ Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

²In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

³A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent⁴, the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- o the "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.⁵;
- o the "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- o the "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

⁴The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

⁵ See, e.g., 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). See also, Rollins Environmental Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

"a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See*, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy", 43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide*.

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	} ⁶	} ⁷
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y ⁸
SKIN SENSITIZATION (ANIMALS)	N	Y ⁹
EYE IRRITATION	N	Y ¹⁰
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y ¹¹
REPRODUCTION STUDY	N	Y ¹²
DEVELOPMENTAL TOX	Y ¹³	Y ¹⁴

⁶43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporting of specific effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical. Unknown effects occurring during such a range test may have to be reported if they are those of concern to the Agency and if the information meets the criteria set forth in Parts V and VII."

⁷Guide at pp. 22, 29-31.

⁸Guide at pp. 34-36.

⁹Guide at pp. 34-36.

¹⁰Guide at pp. 34-36.

¹¹Guide at pp. 22; 36-37.

¹²Guide at pp. 22

¹³43 Fed Reg at 11112

"Birth Defects" listed.

¹⁴Guide at pp. 22

NEUROTOXICITY	N	Y ¹⁵
CARCINOGENICITY	Y ¹⁶	Y ¹⁷
MUTAGENICITY		
<i>In Vitro</i>	Y ¹⁸	Y ¹⁹
<i>In Vivo</i>	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y} ²⁰	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

¹⁵Guide at pp-23; 33-34.

¹⁶43 Fed Reg at 11112
"Cancer" listed

¹⁷Guide at pp-21.

¹⁸43 Fed Reg at 11112; 11115 at Comment 15

"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

¹⁹Guide at pp-23.

²⁰43 Fed Reg at 11112; 11115 at Comment 16.

CAS # 4635-87-4; 592-51-8; 16529-56-9
Chem: 3-Pentenitrile; 4-pentenitrile; 2-methyl-
3-butenitrile
Title: Acute inhalation toxicity
Date: 7/15/70
Summary of Effects: tremors; incoordination

Copies to: J. Mitchell, Jr. (6)
R. S. Taylor (1)

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 301-70 MR NO. 1008

Materials Tested:	1) 3-Pentene nitrile	Haskell Nos.:	1) 5212, 5212-2
	2) 4-Pentene nitrile		2) 5213, 5213-2, 5213-3
	3) 2-Methyl-3-butene nitrile		3) 5214
Materials Submitted by:	R. S. Taylor, Plastics Department Experimental Station	Other Codes:	1) 10712-123-1, none 2) 10614-122, 10614-122, 10614-174-3; 3) 10098-25

ACUTE INHALATION TOXICITY

Procedure: For each exposure, six ChR-CD male rats, weighing 250-289 grams, were exposed to the test material in a 16-liter bell jar for four hours. The test material was metered at a uniform rate into a heated (140-165°C) stainless steel T-tube by a syringe drive and vaporized under pre-urified nitrogen. The test material vapors were mixed with oxygen and carried into the bell jar; house-line air was used as diluent to give the desired atmospheric concentration. For analysis, gas samples were taken periodically from the chamber exit and analyzed by a gas chromatographic method. Gross and histopathologic* examinations were performed on two rats each at 1, 2, 7, and 14 days post-exposure. The other survivors were sacrificed 14 days post-exposure.

Results:

Haskell No.	LC ₅₀ (ppm [†]) [‡]	95% C.L. (ppm [†]) [‡]	Clinical Signs	
			During Exposure	Post-Exposure
5212	420	362- 478	Lethal Conc.: Irregular respiration, hyperemia, red discharge around eyes, tremors, salivation, pale ears; first death within 2½ hours	Death overnight, hypersensitivity, initial weight loss followed by normal weight gain
			Nonlethal Conc.: Irregular respiration, incoordination, red discharge from nose, hindleg tremors	Incontinence, initial weight loss followed by normal weight gain

Results (Cont'd.):

Haskell No.	LC ₅₀ (ppm [†]) [‡]	95% C.L. (ppm [†]) [‡]	Clinical Signs	
			During Exposure	Post-Exposure
5213	2550	2350-2767	<u>Lethal Conc.</u> : irregular respiration, incoordination, lacrimation, salivation, pale ears, tremors, cyanosis, pre-mortem convulsions; first death within 2½ hours	Death overnight, hypersensitivity, weight loss for 1-2 days followed by normal weight gain
			<u>Nonlethal Conc.</u> : irregular respiration, incoordination, hindleg tremors, red discharge from nose	Incontinence, initial weight loss followed by normal weight gain
<hr/>				
5214	3000	2760-3261	<u>Lethal Conc.</u> : irregular respiration, incoordination, lacrimation, salivation, inflamed eyes, red discharge from eyes, hyperemia, tremors, unresponsiveness to sound, pale ears; first death within 3½ hours	Death overnight, initial weight loss followed by normal weight gain
			<u>Nonlethal Conc.</u> : same as above but less severe	Initial weight loss followed by normal weight gain

Pathology: Gross and histopathologic examinations of the rats to either 3-pentene nitrile (H-5213), or 2-methyl-3-butene nitrile (H-5214) showed no anatomical evidence of primary injury. It was apparent that inhalation of these test compounds exerted some sort of stress on the animals, but the nature of this effect was not revealed by microscopic examination of the tissues that were examined.

SUBACUTE INHALATION TOXICITY

Procedure: The acute exposure procedure on Page 1 was used for six test rats. The animals were exposed for four hours each day for two weeks (total of ten exposures). Control rats were exposed to oxygen and nitrogen for the same amount of time. Three control and three test rats were sacrificed after the tenth exposure; the remaining three control and three test rats were sacrificed following a 14-day recovery period.

Results:

Haskell No.	Analytical Concentration (ppm [†])	Mortality Ratio	Clinical Signs	
			During Exposure	Post-Exposure
5212	55	0/6	Mild hyperemia, red discharge around eyes	Normal weight gain
5213	550	0/6	Mild hyperemia, slight irregular respiration	Same as above
5214	560	0/6	Irregular respiration, hyper-sensitivity, red discharge around eyes, salivation, pale ears, pilo-erection during 5th, 6th, and 8th exposures; no weight gain during test period.	Same as above

Pathology: As in the acute tests, gross and histopathologic examinations showed no evidence of primary injury by any of the three test materials.

Summary: The four-hour LC₅₀'s of 3-pentene nitrile (H-5212), 4-pentene nitrile (H-5213), and 2-methyl-3-butene nitrile (H-5214) for young adult ChR-CD male rats are 520 ppm, 2550 ppm, and 3000 ppm, respectively; according to these concentrations 3-pentene nitrile is considered moderately toxic while 4-pentene nitrile and 2-methyl-3-butene nitrile are only slightly toxic by inhalation, but due to their high saturation concentrations, they are potentially hazardous. Clinical signs observed in the rats indicated an effect on the central nervous system. Ten four-hour exposures at 55 ppm (H-5212), 550 ppm (H-5213), and 560 ppm (H-5214) did not give any clinical or pathologic indication of accumulation in exposed rats. There was no histological evidence of primary injury by any of the test materials in any of the tissues[‡] that were examined.

* Tissues examined include: lungs, liver, spleen, kidneys, testes, and thymus.

† ppm are on a volume to volume basis.

‡ Litchfield, J. T., Jr., and F. Wilcoxon. J. Pharmacol. & Expt'l. Therap., 96, 99 (1949).

Experimental Work by: _____

DAVID M. GESSNER

Report by: _____

Donna A. Snee

Approved by: _____

John A. Jaffee

Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12027A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: 0 1 2 pages 1,9 pages _____

Notes:

Contractor reviewer : JW Date: 1/17/96

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # BEHQ 1092-12027 SEQ. A

TYPE (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 02/15/95

CHEMICAL NAME:

CASE#
4635-87-4
592-51-8
16529-56-9

OPTIONAL ACTIONS:

- 0401 NO ACTION REPORTED
0402 STUDIES PLANNED IN INDUSTRY
0403 NOTIFICATION OF WORK IN PROGRESS
0404 LABEL/MSDS CHANGES
0405 PROCESS/ANALYSIS CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

USE:

TOXICOLOGICAL CONCERN:

SPECIES

ONGOING REVIEW

TRIAGE DATA: NON-CBI INVENTORY

LOW
MED
HIGH

RAT

YES (DROP/REFER)
NO (CONTINUE)

YES
NO

CAS SR

REFR

IN TERMINI

1092-12027

12027A

M

3-Pentene nitrile: Acute inhalation toxicity in rats is of moderate concern. Single 4-hour inhalation exposures to ChR-CD male rats yielded an LC_{50} of 420 ppm. Clinical signs included irregular respiration, hyperemia, tremors, salivation, and incoordination during exposure. After exposure, animals given lethal concentrations exhibited hypersensitivity. There were no pathological effects.

M

4-Pentene nitrile: Acute inhalation toxicity in rats is of moderate concern. Single 4-hour inhalation exposures to ChR-CD male rats yielded an LC_{50} of 2,550 ppm. Clinical signs included irregular respiration, incoordination, lacrimation, salivation, tremors, cyanosis, and convulsions during exposure. After exposure, animals given lethal concentrations exhibited hypersensitivity. There were no pathological effects.

M

2-Methyl-3-butene nitrile: Acute inhalation toxicity in rats is of moderate concern. Single 4-hour inhalation exposures to ChR-CD male rats yielded an LC_{50} of 3,000 ppm. Clinical signs included irregular respiration, incoordination, lacrimation, salivation, hyperemia, tremors, and unresponsiveness to sound during exposure. There were no pathological effects.

L

3-Pentene nitrile: Subacute inhalation toxicity in rats is of low concern. Six male ChR-CD rats were exposed to 55 ppm, 4 hours/day for a total of 10 exposures over two weeks. There were no deaths. Clinical signs included mild hyperemia during exposure. There were no pathological effects.

L

4-Pentene nitrile: Subacute inhalation toxicity in rats is of low concern. Six male ChR-CD rats were exposed to 550 ppm, 4 hours/day for a total of 10 exposures over two weeks. There were no deaths. Clinical signs included mild hyperemia and slight irregular respiration during exposure. There were no pathological effects.

L

2-Methyl-3-butene nitrile: Subacute inhalation toxicity in rats is of low concern. Six male ChR-CD rats were exposed to 550 ppm, 4 hours/day for a total of 10 exposures over two weeks. There were no deaths. Clinical signs included irregular respiration, hypersensitivity, salivation, and piloerection during exposure. There were no pathological effects.